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Associations between Race, Menthol, and Acute Tobacco Withdrawal

by

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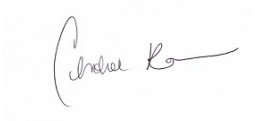

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Cendrine Robinson

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ABSTRACT

Associations between Race, Menthol, and Acute Tobacco Withdrawal:

Cendrine Robinson, MS, 2013

Thesis directed by: Andrew Waters, Associate Professor, Medical & Clinical Psychology

African Americans experience greater tobacco-related morbidity and mortality than Caucasians, have greater difficulty quitting tobacco than Caucasians, and are more likely to smoke mentholated cigarettes than Caucasians. The mechanisms underlying racial differences in smoking cessation are not clear and scant research has investigated the effect of race and menthol smoking on acute tobacco withdrawal. This study investigated whether African-American (n = 104) and Caucasian smokers (n = 99) differed in abstinence-induced changes in self-report, physiological, and cognitive performance measures. Smokers not wishing to quit completed two counterbalanced experimental sessions. Before one session they abstained from smoking for 12 hours, and before the other session they smoked normally.

African Americans were more likely to smoke menthol cigarettes than Caucasians. African Americans reported smaller abstinence-induced changes on subjective measures, including the total scores of the Questionnaire for Smoking Urges (QSU) and the Wisconsin Withdrawal Smoking Scale (WSWS). Compared to Caucasians, African

Americans reported higher ratings of craving and withdrawal at the non- abstinent session, but there was no such difference during the abstinent session. There were no effects of race on abstinence-induced changes in electroencephalogram measures or cognitive performance. Caucasian participants who smoked menthol cigarettes did not generally exhibit greater abstinence-induced change scores than Caucasian participants who smoked non-menthol cigarette. In summary, there was no evidence that African Americans experience greater acute tobacco withdrawal than Caucasians, or that menthol smokers experience greater acute tobacco withdrawal than non-menthol smokers.

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CHAPTER 1: Introduction

PREVALENCE OF TOBACCO USE

Tobacco use continues to be a major health concern in the United States. Despite significant declines in the past 30 years, approximately 27.4% of individuals aged 12 and older are current users (past month use) of tobacco products (CDC, 2011). Furthermore, the rate of decline in tobacco use has slowed dramatically since 2002 (SAMSHA, 2008). The use of cigarettes in the U.S is particularly concerning because in 2010 the smoking rate among adults 18 and older was 20% (CDC, 2011).

TOBACCO AND HEALTH

These rates are alarming because tobacco use has been linked to multiple cancers, cardiovascular disease, pulmonary disease, and the exacerbation of other illnesses (CDC, 2010; Sasco, Secretan, & Straif, 2004; Gandini et al., 2008). The perniciousness of tobacco use is evident from over five decades of research (Musk & De Klerk, 2003). For instance, in 1964 an advisory committee to the U.S. Surgeon General reported that there is a causal relationship between smoking and lung cancer (U.S. Department of Health Education and Welfare, Public Health Service, 1964). Since the publication of the 1964 Surgeon General's report, there have been hundreds of studies supporting the link between tobacco and cancer (Sasco et al., 2004; Gandini et al., 2008). Despite this evidence, tobacco continues to be the leading cause of preventable morbidity and mortality in the U.S. (CDC, 2010). Approximately 435,000 individuals die from tobacco-related illnesses per year (3). The significance of this problem has been noted by the U.S. Department of Health and Human Services (USDHHS) in Healthy People 2020. This

report presented a goal of reducing tobacco use to less than 12% by 2020 (CDC, 2010). Given that the rate of decline has slowed dramatically and tobacco use costs the U.S. 96 billion dollars in medical costs per year, expanded efforts are needed to reduce tobacco smoking (CDC, 2010).

TOBACCO AND HEALTH DISPARITIES

The health consequences of tobacco use are far reaching and affect all demographics. However, there are subgroups within the U.S. population that are disproportionately impacted, such as racial/ethnic minorities and individuals with low socioeconomic status (Fagan, 2004). For instance, African Americans have the highest rates of tobacco related morbidity and lower rates of smoking cessation (Moolchan et al., 2007; USDHHS, 1998). As noted in the USDHHS Healthy People 2020, studying disparities among subgroups in the U.S. is a priority (CDC, 2010).

Differences in morbidity and cessation outcomes among African Americans (and some other subgroups) can be classified as health disparities. There is not a consensus on how to define health disparities. However, the National Institutes of Health described health disparities as "…differences in the incidence, prevalence, mortality, and burden of disease and other health consequences among a specific population" (NIH, 2000, p. 3). These differences are typically associated with some level of inequality (Carter-Pokras & Baquet, 2002). For instance, some subgroups (e.g., racial/ethnic minorities, women, disabled) have a history of social, economic, educational, and political inequality (Fagan, Moolchan, Lawrence, Fernander, & Ponder, 2007). Additionally, it is important to consider that there is heterogeneity within subgroups. Within group differences are explained by a variety of factors including gender, marital status, and financial resources

(Moochlan et al., 2007). Therefore, within group and between group differences should be examined when addressing health disparities.

The history of marginalization of subgroups and the disproportionate rates of tobacco use, morbidity, and cessation among groups such as African Americans suggest that studies on specific groups are necessary. Furthermore, it is evident that subgroups have been understudied in the tobacco literature (Fagan et al., 2007; Moolchan et al., 2007). Specifically, there is limited knowledge on patterns of use, cessation, and withdrawal among African American smokers. As a result, there is little research examining factors that may contribute to between-race differences in cessation rates and other tobacco-related health disparities (Fernander, Shavers, & Hammons, 2007).

USE OF RACIAL CATEGORIES

Before examining differences between subgroups, it is important to note that research in race-related health disparities should be done with caution because it requires categorizing individuals into groups based on race. The categorization of individuals by race has a negative history in the U.S., particularly as it relates to prejudice and discrimination. Furthermore, methodological advances in molecular biology provide evidence that humans are genetically homogeneous (Jorde & Wooding, 2004). The variations that do exist are geographically structured as a result of the isolation of groups, millions of years ago (Jorde & Wooding, 2004). This evidence suggests that classification of individuals into races is purely for socio-political purposes. Hence, a great deal of controversy exists among researchers and laypeople regarding how (or if) individuals should be categorized (Jorde & Wooding, 2004). For the purpose of this paper, race was used to distinguish individuals who self-identify with a specific cultural group and

ancestral geographical location. The terms used to describe races are aligned with those used by the U.S. Department of Health and Human Services' (USDHHS) report on smoking among racial/ethnic groups (USDHHS, 1998). Moreover, these classifications are used with the intent of increasing the body of knowledge available on health disparities in smoking. It should be noted that the Office of Management and Budget guidelines on terminology for race and ethnicity have changed since the data were collected (i.e., Caucasian should be referred to as White; OMB, 2003).

AFRICAN AMERICANS AND CIGARETTE SMOKING

Health disparities in African Americans are of particular interest because African Americans bear the burden of smoking-related disease, despite there being a similar prevalence of African-American and Caucasians smokers (Haiman et al., 2006; USDHHS, 1998; Siegel et al., 2011). A recent epidemiological study of cancer risk and cigarette use among Hispanics, African Americans, Caucasians, and Native Americans reported that African Americans and Native Americans were more susceptible to lung cancer than other groups (Haiman et al., 2006). These differences existed among light (<10 cigarettes per day) and heavy (11 to 30 cigarettes per day) smokers. Furthermore, African Americans have a higher mortality rate from lung cancer than any other racial/ethnic group (Siegel et al., 2011). For instance, the death rate from lung cancer is 1.28 times higher among African American men then Caucasian men (Siegel et al., 2011). Similarly, African Americans smokers are more susceptible to cardiovascular diseases than are other groups (USDHHS, 1998).

The alarming rates of morbidity among African Americans have been well documented. As a result, the Surgeon General Report on Tobacco Use among U.S.

Racial/Ethnic Minority Groups identified tobacco related health disparities among African Americans as a national health priority (USDHHS, 1998).

AFRICAN AMERICANS AND SMOKING CESSATION

In addition to suffering from greater tobacco-related morbidity, African American smokers have greater difficulty quitting tobacco (Trinidad, Perez-Stable, White, Emery, & Messer, 2011). For example, the Surgeon General report indicated that 35.4% of African Americans reported long-term cessation compared to 50.5% of Caucasians (USDHHS, 1998). Table 1 reviews the studies that have examined differences in smoking cessation among African Americans and Caucasians. The table includes studies that were published between 2000 and 2011. Ten studies were found that addressed this question (there were eight publications; Rabius et al. [2011] and Piper et al. [2010] published two studies in one paper)

Four of the studies involved the analysis of large-scale survey data, without a systematic tobacco cessation intervention. In these studies, cessation rates were compared for African American and Caucasian smokers. For instance, Trinidad and colleagues (2011) conducted a logistic regression to examine the effect of race on cessation six months later utilizing data from the Tobacco Use Supplement to the Current Population Survey (n = 141,603). They found that the odds of quitting for at least six months was 49% lower for African American smokers. Among the other three survey studies, two reported lower cessation rates for African Americans (Trinidad, Gilpin, White, & Pierce, 2005; Fu, et al., 2008b). One study found significantly lower cessation rates among African Americans, but the difference was eliminated after controlling for sociodemographic differences (King et al., 2004).

Six studies assessed the effects of various interventions, including quit lines, nicotine replacement therapy, and bupropion. The authors of these studies assessed for racial differences in the effectiveness of the interventions. There were mixed findings among these studies. Four studies indicated that there were no differences in smoking cessation rates among African Americans and Caucasians (Rabius, Wiatrek, & McAlister, 2011; Fu et al., 2008b; Piper et al., 2010). Conversely, two studies found differences between African Americans and Caucasians. Piper and colleagues (2010) examined racial differences in an efficacy trial of several pharmacotherapies including bupropion, nicotine lozenges, and nicotine patches (study 1). They found lower cessation rates among African American smokers (Piper et al., 2010). Similarly, Covey and colleagues (2008) found lower cessation rates among African American smokers. In this study participants received an eight week trial of bupropion, the nicotine patch, and counseling.

It is difficult to draw conclusions about the effect of race on cessation in the intervention studies because the interventions varied (e.g., some studies used quit-lines while other used medication). Future research on racial differences in cessation rates for medication, quit lines, and counseling is necessary. Overall, this review suggests that differences in cessation among African Americans and Caucasians are detectable in large-scale survey studies. However, to date there has been little research examining factors that may mediate between-race differences in cessation. In the following section, the role of nicotine withdrawal as a potential mediator is examined.

NICOTINE ADDICTION AND WITHDRAWAL

The nicotine withdrawal syndrome may potentially explain differences in cessation outcomes among African Americans and Caucasians. As will be discussed below, there are behavioral and biological differences among African Americans and Caucasians that may affect the withdrawal experience. Before these differences are examined, it is important to briefly review the effects of nicotine and the withdrawal syndrome.

ACTIONS OF NICOTINE IN THE CENTRAL NERVOUS SYSTEM

Nicotine addiction is a chronic, relapsing brain disorder characterized by compulsive use, despite harmful consequences, and the appearance of withdrawal symptoms upon cessation (Leshner, 1997; USDHHS, 1988). The pharmacological actions of nicotine have been well-studied and are important to understand prior to examining withdrawal. The actions of nicotine are complex, and a detailed review is beyond the scope of this paper. However, a brief summary is provided.

Nicotine acts on nicotinic acetylcholine receptors (nAChRs) distributed throughout the central nervous system (Goldberg, 1981). Nicotine binds to the α4B2 subunit of the nAChR complex in the Ventral Tegmental Area (VTA), an area of the midbrain associated with the motivational effects of drugs of abuse (Millar & Gotti, 2009). After nicotine binds to nAChR receptors in the VTA, the ascending neurons of the VTA project to the nucleus accumbens, corpus striatum, and the prefrontal cortex, which causes dopamine to be released in these areas (Grunberg & Starosciak, 2010). Nicotine modulates the release of other neurotransmitters such as norepinephrine, vasopressin, acetylcholine, serotonin, and B-endorphin. These

transmitters are involved with the pleasurable psychoactive effects of nicotine such as arousal, cognitive enhancement, mood modulation, and appetite suppression (Berrendero, Robledo, Trigo, Martín-García, & Maldonado, 2010).

In chronic smokers, nicotine reduces the activity of Monoamine Oxidase A and B, which are enzymes that break down dopamine and norepinephrine (Benowitz, 2008). Reduced enzyme activity increases the amount of dopamine and norepinephrine in the synapses, by preventing breakdown of neurotransmitters. Elevated levels of neurotransmitters contribute to the development of nicotine dependence. Repeated nicotine administration results in neuroadaptations such as the upregulation of nAChrs in response to desensitized receptors (Benowitz, 2008).

The nicotine withdrawal syndrome occurs during periods of abstinence. When a smoker abstains, nicotine is eliminated from the body and smokers experience symptoms that are opposite to what they experience when using nicotine. For instance, smokers may experience cognitive, physiological, and affective symptoms such as increased hunger, difficulty concentrating, and irritability (Hughes, 2007a).

Nicotine dependence is believed to develop from positive reinforcement (e.g., mood and cognitive enhancement) negative reinforcement (e.g., motivation to relieve withdrawal symptoms), and the conditioning of stimuli associated with use (Grunberg, Berger, & Starosciak, 2011; Benowitz, 2008). The latter warrants elaboration because theories suggest that the ability of conditioned stimuli to trigger motivational responses is a key element of addiction (Robinson & Berridge, 1993).

The use of nicotine is reinforced by strong associations between smoking and environmental or internal cues (Robinson & Berridge, 1993). As noted in Robinson & Berridge's Incentive Sensitization Theory, drug cues become so salient that they cause drugs to be wanted independent of any pleasure they yield (Robinson & Berridge, 2008). This theory suggests that the conditioning of drug cues with neutral cues triggers a motivational response for drugs (Robinson & Berridge, 2008). This theory is of particular relevance because it suggests that drug dependent individuals should exhibit selective attention toward drug cues. There is evidence that smokers have a selective attention to smoking cues (i.e., attentional bias; Waters et al., 2003). Therefore, to thoroughly examine withdrawal symptoms, it is important to assess for elevations in attention to drug cues.

NICOTINE WITHDRAWAL

Abstinence from tobacco has been found to produce subjective, physiological, and cognitive changes (Hatsukami, Hughes, & Pickens, 1985; Hughes, Keenan, & Yellin, 1989; Hughes, 2007a). Subjective symptoms include negative affect, irritability, difficulty concentrating, craving, anxiety, and dysphoria (American Psychiatric Association, 2000; Hughes, Gust, Skoog, & Keenan, 1991; Hughes, 2007a). The primary physiological/somatic symptoms are bradycardia, hyoptension, increased appetite, and gastrointestinal discomfort (Hatsukami, Hughes & Pickens, 1985; Kenny & Markou, 2000). Abstinence from tobacco also affects objective cognitive performance as documented by decrements in performance on tasks of sustained attention (Hughes, Keenan, & Yellin, 1989; Leventhal et al., 2010).

There are also abstinence-induced changes in brain activity as detected by electroencephalogram (Pickworth et al., 1989). The electroencephalogram (EEG) is a non-invasive tool that can be used to measure abstinence-induced changes in the central nervous system. Previous research has demonstrated EEG changes following overnight abstinence (Herning et al., 1983; Knott & Venables, 1977; Pickworth, et al. 1989). For example, abstinent smokers exhibit increases in theta power (associated with diminished arousal) and decreases in alpha power (associated with drowsiness) compared to non-abstinent smokers (Herning et al., 1983; Pickworth, et al. 1989).

Research suggests that the acute tobacco withdrawal syndrome is an important component of nicotine addiction. For instance, withdrawal symptoms are used in the DSM-IV-TR criteria to diagnose nicotine addiction (American Psychiatric Association, 2000). Furthermore, there is evidence indicating that greater withdrawal symptoms are prospectively associated with poorer cessation outcomes (Piasecki, Jorenby, Smith, Fiore, & Baker, 2003a; Kenford et al., 2002). In the past, studies reported that there was not a consistent relationship between withdrawal and cessation (Patten & Martin, 1996). However, more recent evidence suggests that previous studies did not capture the variability of withdrawal symptoms (Piasecki et al., 2000). Piasecki and colleagues demonstrated that creating subgroups of withdrawal profiles clarified the relationship between withdrawal and relapse (Piasecki et al., 2000). Researchers have used alternative statistical techniques (hierarchical linear modeling) to further demonstrate that the withdrawal syndrome is associated with relapse (Piasecki et al., 2003a). This research suggests that the withdrawal syndrome is an important aspect of addiction and should be explored when examining racial differences in tobacco use.

The inability of older studies to demonstrate a strong link between withdrawal and cessation may also be related to the fact that studies failed to assess the salience of drug cues during abstinence. As previously stated, research suggests that drug cues are critical for the maintenance of drug dependence (Robinson & Berridge, 2008). Waters et al. (2003) demonstrated that individual differences in attentional bias in abstinent smokers predicted relapse in a subsequent smoking cessation attempt. Similar findings have been reported in other addiction studies (Janes et al., 2010; Marissen et al., 2006; Carpenter, Schreiber, Church, & McDowell, 2006). This evidence suggests that attentional bias should be assessed when evaluating withdrawal.

AFRICAN AMERICANS AND NICOTINE WITHDRAWAL

Assessing the nicotine withdrawal syndrome among African American smokers may be helpful in understanding racial differences in tobacco cessation. Little research has previously investigated the withdrawal syndrome among African American smokers. However, there are several behavioral and biological factors that suggest that African Americans smokers may experience more intense withdrawal symptoms.

First, African American smokers have a higher carbon monoxide boost (increase in CO level associated with smoking) and higher nicotine intake per cigarette (1; 2; 4). Second, African Americans prefer cigarettes that are higher in nicotine content (Pérez-Stable et al., 1998). Third, there are differences in cotinine (the major metabolite of nicotine) levels (Caraballo et al., 1998). Caraballo and colleagues examined cotinine in blood specimens of African American and Caucasian smokers who smoked *ad libitum*.

African American smokers had higher levels of cotinine in their blood after controlling for the number of cigarettes smoked per day and environmental tobacco exposure (Caraballo et al., 1998). This difference in cotinine levels may be explained by differences in nicotine metabolism or nicotine intake (Pérez-Stable et al., 1998; Caraballo, et al., 1998). For instance, one study reported that the half-life of cotinine, the major metabolite of nicotine (Keenan et al., 1994), was 950 and 1,064 minutes for Caucasians and African Americans respectively (Pérez-Stable et al., 1998). It was also reported that African American smokers took in 30% more nicotine per cigarette (Pérez-Stable et al., 1998).If African Americans smoke each cigarette more intensely than Caucasians, smoke cigarettes with a higher nicotine yield, and metabolize nicotine more slowly, then their brains may be more exposed to more nicotine. Greater nicotine exposure may lead to greater nicotine withdrawal.

MENTHOLATED CIGARETTES

Another striking difference between African American and Caucasian smokers is the preference of African American smokers for menthol cigarettes. Approximately 68% - 80% of African Americans smokers consume cigarette brands that contain the tobacco additive menthol, compared to 20-22% of Caucasian smokers (Giovino, Sidney, Gfroerer, O'Malley, Allen, Richter, & Cummings, 2004). This implies that menthol may influence nicotine dependence and the health consequences of smoking.

Mentholated cigarettes have come under heightened scrutiny of researchers and policymakers following a 2009 ban of cigarette flavors (e.g., additives such as cloves) with the exception of menthol (FSPTC, 2009). Approximately 25% of the cigarette packs sold in the U.S. are of the menthol variety (Giovino et al., 2004). It is

noteworthy that 90% of cigarettes sold in the U.S. contain a small amount of menthol (0.03% of the tobacco weight); however, brands that are marketed as menthol contain 0.1% to 1% (Giovino et al., 2004). The major component of menthol is monocylic terpene alcohol, which is a compound derived from peppermint oil. Menthol stimulates transient receptor potential channels (thermoreceptors in the mouth and throat) that evoke thermal and pain sensations (Gelal, Jacob, Yu, & Benowitz, 1999; Harris, 2006). Some researchers have argued that the cooling effect of menthol is associated with a perception of a less harsh taste, thereby facilitating greater inhalation (Hymnowitz, Mouton, & Edkholdt, 1995). Furthermore, menthol produces carcinogenic compounds such as benzopyrenes, which have been posited as potentiating the harmful effects of cigarettes (Schmeltz & Schlotzhauer, 1968). Additionally, mentholated cigarettes are higher in tar and nicotine than non-menthol cigarettes (FTC, 2000).

MENTHOL AND HEALTH

There is a growing body of research examining effects of menthol on tobacco related morbidity (Sidney, Tekawa, Friedman, Sadler, & Tashkin, 1995; Kabat & Herbert, 1991). In an epidemiological study, Sidney et al. (1995) reported that the relative risk of lung cancer was 1.45 (95% CI: 1.03 to 2.02) for men who smoked menthol cigarettes compared to men who smoked non-menthol cigarettes. Moreover, this effect persisted when controlling for age, education, the number of cigarettes smoked per day, and duration of smoking. Similarly, a study by Çiftçi and colleagues (2008) examined the acute effects of mentholated cigarettes on cardiovascular function and reported that mentholated cigarettes were associated with additional detrimental effects on right ventricular tissue. Conversely, several studies suggest that menthol cigarettes are not

more harmful than traditional cigarettes (Carpenter, Jarvik, Morgenstern, McCarthy, & London, 1999; Pletcher, Hulley, Houston, KiefeI, Benowitz, & Sidney, 2006; Kabat & Hebert, 1991; Blot et al., 2011). For instance, a study of 1,535 smokers assessed the effects of menthol on atherosclerosis and pulmonary function. There were no differences in tobacco-related coronary calcification or 10-year pulmonary function (Pletcher et al., 2006). Similarly, Blot et al. (2011) found that menthol preference did not contribute to higher incidences of lung cancer cases. Therefore, the evidence of a direct link between menthol and health risk is inconclusive.

MENTHOL AND CESSATION

Researchers have also examined the relationship between menthol and smoking cessation. Menthol cigarettes are believed to lead to greater dependence due to their cooling effect, alleviation of irritation, and higher tar content (Giovino et al., 2004; Gartern & Faulkner, 2002). To examine the effect of menthol on cessation, Gunderson and colleagues (2009) conducted an analysis of a sample of 7815 Caucasian, African American, and Hispanics who were former smokers. There were significant race by menthol interactions. In particular, non-Caucasian (African American and Hispanic combined) menthol smokers had poorer cessation outcomes compared to non-Caucasian non-menthol smokers, but the same was not true for Caucasian smokers. Similarly, Harris and colleagues (2004) examined the association between menthol status and cessation in a study assessing predictors of cessation with 600 African American smokers who used bupropion (Harris et al., 2004). The authors reported that menthol use decreased the likelihood of quitting successfully.

Several other studies corroborate these findings, suggesting that menthol affects smoking cessation outcomes among African Americans and Hispanics (Foulds, Hooper, Pletcher, & Okuyemi, 2010). For instance, Foulds and colleagues (2010) conducted a systematic review of studies that examined the relationship between menthol status and cessation rates among non-Caucasian and Caucasian smokers. There were no consistent effects of menthol among Caucasian smokers. However, there is evidence that menthol affects cessation among non-Caucasian and adolescent smokers (Gandhi, Foulds, Steinberg, Lu, & Williams, 2009; Gundersen et al., 2009; Okuyemi, Faseru, Cox Sanderson, Bronars, & Ahluwalia, 2007).

MENTHOL AND NICOTINE METABOLISM

The effect of menthol on nicotine metabolism and tobacco constituent (nicotine and carbon monoxide) exposure has also been examined. This question was examined in a small study of African American and Caucasian smokers (Benowitz, Herrera, & Jacob, 2004). Menthol inhibited the metabolism of nicotine in African American and Caucasian smokers (clearance: 1289 ml/min for non-menthol versus 1431 ml/min for menthol). However, this study did not find any effect of menthol on exposure to tobacco smoke. There is evidence that among African American light smokers (less than 10 cigarettes per day), those who smoke menthol cigarettes have slower metabolism of nicotine than non-menthol smokers (Ho et al., 2009). There is also evidence from an *in vitro* study, that menthol inhibits CYP2A6, an enzyme involved with the oxidation of nicotine and cotinine, thereby impeding nicotine metabolism (MacDougall, Fandrick, Zhang, Serafin, & Cashman, 2003). It has been proposed that the delay in nicotine metabolism allows additional time for nicotine to bind to receptors (Hoffman, 2011). However, research on

the effect of menthol on nicotine metabolism is inconclusive because several studies have found no relationship between menthol and nicotine metabolism (Ahijevych, 2002; Mustonen, Spencer, Hoskinson, Sachs, & Garvey, 2005; Signorello, Cai, Tarone, McLaughlin, & Blot, 2009).

In sum, while it is unclear if menthol has effects on health, there appears to be an association between menthol and cessation among African American smokers. Therefore, it is important to consider the effect of menthol when examining racial differences in withdrawal.

RATIONALE FOR THE CURRENT STUDY

To summarize, African Americans experience greater cigarette smoking-related morbidity and mortality than Caucasians. In addition, African Americans have greater difficulty quitting tobacco than Caucasians. However, the mechanisms underlying racial differences in smoking cessation are not clear. Given the between-race differences in smoking behavior noted earlier (e.g., deeper inhalation, higher nicotine intake per cigarette, and preference for menthol cigarettes in African Americans), African Americans may be exposed to larger doses of nicotine. African Americans may experience greater nicotine-induced neuroadaptations and, therefore, differ in their experience of the nicotine withdrawal syndrome. Notably, little previous research has investigated racial differences in withdrawal. This was the primary aim of the current study. A secondary aim was to examine the effect of menthol on nicotine withdrawal.

The present study is a secondary analysis of data collected from 2001 to 2004 at the National Institute of Drug Abuse Intramural Research Program. Abstinence-induced changes were examined in adult African American and Caucasian smokers not trying to

quit smoking. Nicotine withdrawal was assessed using subjective, physiological, and cognitive measures. The specific aims and hypotheses were as follows:

SPECIFIC AIMS AND HYPOTHESES

Specific Aim 1: To examine between-race differences in acute tobacco withdrawal symptoms in African Americans and Caucasians.

Hypothesis 1.1: African Americans will report greater abstinence-induced changes than Caucasians on self-report measures of withdrawal.

Hypothesis 1.2: African Americans will exhibit greater abstinence-induced changes than Caucasians on physiological assessments of withdrawal.

Hypothesis 1.3: African Americans will exhibit greater abstinence-induced changes than Caucasians on cognitive measures of withdrawal.

Specific Aim 2: To explore the effect of menthol on withdrawal symptoms in smokers.

Hypothesis 2.1: Menthol smokers will report greater abstinence-induced changes than non-menthol smokers on self-report measures of withdrawal.

Hypothesis 2.2: Menthol smokers will exhibit greater abstinence-induced changes than non-menthol smokers on physiological assessments of withdrawal.

Hypothesis 2.3: Menthol smokers will exhibit greater abstinence-induced changes than non-menthol smokers on cognitive measures of withdrawal.

CHAPTER 2: Method

PARTICIPANTS

Participants were 104 African American and 99 Caucasian smokers recruited from the Baltimore area via newspaper and radio advertisements. Other data from this sample have been reported elsewhere (Heishman et al., 2008; Leventhal et al., 2007; Leventhal et al., 2010). The inclusion criteria were: aged 18 years or older; currently smoking at least 15 cigarettes per day; smoked for at least two years; score 3+ on the Fagerström Nicotine Dependence Scale (FTND); and smoke a brand of cigarettes that delivers at least 11.0 mg tar and 0.7 mg nicotine as rated by the Federal Trade Commission method. The exclusion criteria were: history of a serious medical condition (e.g., myocardial infarction, heart failure, angina, stroke, diabetes, hypertension); treatment with nicotine replacement products within the past six months; use of antidepressants in the past year; use of any smoking cessation treatment within the past six months; pregnant or nursing; and an estimated IQ of < 78 on the Shipley Institute of Living Scale (Shipley, 1940). Information about medical conditions, tobacco use, and past cessation treatment was obtained from participant self-report. The exclusion criteria were used to confirm that the participants were in good health and would not endure adverse consequences from participating in the study. Also, the criteria excluded individuals who used nicotine replacement products to ensure that withdrawal effects would not be affected by medications. The National Institute on Drug Abuse Intramural Research Program (NIDA IRP) Institutional Review Board approved the study.

As reported in Leventhal et al. (2007), 858 participants completed a medical screening visit; 521 were ineligible due to inclusion/exclusion criteria. Of the 337 eligible

participants, 230 attended an orientation session, and 209 completed the two experimental sessions (an abstinent and a non-abstinent session). However, six participants did not meet criteria for biochemical confirmation of cigarette smoking and were excluded from analyses (see below). Demographic and cigarette smoking characteristics of the final sample are reported in Table 1.

BIOCHEMICAL VERIFICATION

For the abstinent session, abstinence was verified using expired carbon monoxide (CO) levels. Participants were considered non-abstinent (i.e., non-compliant) if they reported smoking within the past 12 hours or if they had CO levels greater than 11 ppm. Individuals with a CO greater than 11 ppm were permitted to re-schedule their abstinent session (*SRNT Subcommittee on Biochemical Verification, 2002)*. At the abstinent session, mean CO levels were 7.3 ppm (*SD* = 2.5) and 6.6 ppm (*SD* = 2.5) for Caucasians and African Americans respectively.

For the non-abstinent session, six participants had CO levels lower than 10 ppm and were excluded from the analysis. They were excluded because CO levels below 10 ppm suggested either that they do not smoke 15 or more cigarettes per day, or that they did not comply with the instructions to smoke normally before the non-abstinent session (*SRNT Subcommittee on Biochemical Verification, 2002)*. At the non-abstinent session, mean CO levels were 31.6 ppm (*SD* = 13.2) and 28.4 ppm (*SD* =10.8) for Caucasians and African Americans, respectively. The abstinence-induced change in CO levels did not differ by race (Caucasians: *M* = -24.3 ppm, *SD* = 12.4, African Americans: *M* = -21.9 ppm, *SD* = 10.3; $t(198) = 1.52, p > .1$).

PROCEDURE

In the parent study, individuals participated in a preliminary phone interview to assess tobacco use and medical conditions. Eligible participants were invited to attend a screening at NIDA IRP to further assess several medical and psychological variables. Assessments included the Addiction Severity Index (ASI; McLellan et al., 1992), Shipley Institute of Living Scale (Shipley, 1940), and the Symptom Check List-90 (Derogatis, 1992). Self-reported race was obtained by an item on the ASI: "Of what race/ethnicity do you consider yourself?" Participants selected from the following options (one selection only): Caucasian (not Hispanic); African American (not Hispanic); American Indian; Alaskan Native; Asian/Pacific Islander; Hispanic-Mexican; Hispanic-Puerto Rican; Hispanic-Cuban; and Other Hispanic. The classifications for race are aligned with terms that most groups find appropriate as noted by the USDHHS (USDHHS, 1998). Participants could endorse only one item and those who endorsed either of the first two options were eligible for this study. Participants were also asked to indicate whether their preferred brand of cigarette was "menthol" or "non-menthol" on a self-report tobacco history questionnaire. A physician conducted the physical examination and reviewed the patient's health history.

Eligible participants attended a 90-minute orientation session, followed by two counterbalanced 60-minute experimental sessions (abstinent, non-abstinent). The three sessions occurred on three different days. The mean number of days between experimental sessions was 2.7 days (SD =2.9) and 3.1 days (SD = 4.8) for Caucasians and African Americans respectively, $t(201) = -0.67$, $p = .50$. Participants completed demographic and smoking history questionnaires at the orientation session, as well as

Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991). At the orientation session, they smoked *ad libitum* before and after the session.

Participants were asked to smoke *ad libitum* within 20 minutes of the non-abstinent session. The average reported time since their last cigarette was on average 15.7 minutes (*SD* = 10.7) before this session. The mean reported time was 15.3 minutes (*SD* =9.7) and 16.0 minutes (*SD* = 11.8) for Caucasians and African Americans respectively, $t(201) = -0.45$, $p = .65$. For the abstinent session, participants were asked to refrain from smoking for the 12-hr period before the session. The order of the sessions was counterbalanced across participants. The experimental sessions were scheduled in the afternoons. The research staff attempted to schedule the two experimental sessions at the same time of day. Self-report, physiological, and cognitive assessments (detailed below) were administered at the two experimental sessions.

MEASURES

Subjective Assessments

The 11-item Minnesota Nicotine Withdrawal Scale (MNWS; Hughes & Hatsukami, 1986) assessed withdrawal symptoms on a six-point Likert scale. This measure assesses withdrawal symptoms listed in the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV-TR;* American Psychiatric Association, 2000). It has been validated using factor analysis in a number of studies and is a reliable measure, with a Cronbach's *alpha* of .80 (Toll, O'Malley, McKee, Salovey, & Krishnan-Sarin, 2007). Exploratory and confirmatory factor analysis revealed that this measure is also valid in African American smokers (Krigel, 2007).

The 23-item Wisconsin Smoking Withdrawal Scale (WSWS; Welsch, Smith et al., 1999) assessed six subscales of nicotine withdrawal (anxiety, anger, hunger, concentration problems, craving, and sadness), and a total withdrawal score. This scale is sensitive to smoking withdrawal and is reliable, with Cronbach's *alph*as ranging from .75 to .93 for the subscales (Welsch et al., 1999). Factor analysis and regression analyses indicate that the WSWS is valid for African American smokers (Castro et al., 2011)

The 10-item Brief Questionnaire of Smoking Urges (QSU; Cox, Tiffany, & Christen, 2001) is a questionnaire used to assess the intention and desire to smoke (Factor 1), and desire for smoking to reduce negative affect (Factor 2). A total craving score can also be computed. This measure has high reliability for both factor 1 and factor 2 (Cronbach's alpha = .95 and .93, respectively; Cox, Tiffany, & Christen, 2001). An exploratory factor analysis suggests that this measure is valid for African American smokers (Clausius et al., 2010).

The 20-item Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988) assessed positive and negative affect (Watson et al., 1988). The measure has two scales (Positive Affect, Negative Affect) both of which have good internal consistency (Cronbach's alpha > .80) and excellent convergent and discriminant validity (Watson et al., 1988).

The 8-item Hunger Questionnaire assessed hunger on 10-point Likert scales (Hill and Blundell, 1982). Participants rated their feelings of hunger, fullness, and desire to eat (1 = not at all, 10 = extremely).

The 8-item Subjective Attentional Bias Questionnaire (SBQ) assessed the extent to which participants felt that their attention was captured by tobacco cues (Leventhal et

al., 2007). This measure was constructed by the authors of the parent study. Notably, the abstinence-induced change scores on the eight items were strongly inter-correlated (Cronbach alpha = 0.88) and the SBQ total score (mean of eight items) was greatly increased by abstinence (effect size $d = 1.23$, $p < .001$) (Leventhal et al., 2007).

Physiological Assessments

Heart rate, systolic blood pressure, and diastolic blood pressure were measured using the electronic Datascope machine. Electroencephalogram (EEG) recordings were collected from Fz, Pz, and Cz electrodes using the Biologic analysis system (Biologic Instruments, Chicago, IL). EEG frequency was computed as the frequency (Hz) at which 80% power of the band had accumulated (resolution, 0.5 Hz) in each of the usual clinical frequency bands: delta, 0.5-3.5 Hz; theta, 4.5-7.5 Hz; alpha, 8.5-12.5 HZ; beta 1, 14.5-23.5 Hz, and beta 2, 25-31.5 Hz. Data were collected at one minute intervals (eyes closed and eyes open), and were aggregated over the three electrodes.

Cognitive Assessments

The Two-Letter Search Task (ST) and the Serial Math Task (MT), from the Walter Reed Performance Assessment Battery, assessed cognitive performance (Thorne, Genser, Sing, & Hegge, 1985). The ST assessed visual scanning, attention capabilities, and recognition. In the ST, the participant viewed two target letters on the computer screen and a string of twenty letters on the bottom of the screen. Participants were instructed to respond by pressing one key if the target letters were in the string and another key if the target letters were not in the string. The task consists of 20 trials and takes approximately 2 minutes. The Serial Math Task (MT) assessed mathematical reasoning. For the MT, participants were presented with two random digits for 250

milliseconds. The numbers were followed by a plus sign, minus sign, or question mark. The participants were instructed to perform a mathematical operation and to enter the final digit as quickly as possible (e.g., the correct response to 7 + 5 is 2, because the 2 is the final digit of 12). The task consisted of 250 trials and took about 4 minutes to complete. The mean reaction times (of correct responses) and the error rates were analyzed.

The Digit Symbol Substitution Task (DSST) assessed psychomotor performance. Participants were required to press a computer key to reproduce symbols presented on a computer monitor during a 90 second period. The correct number of reproduced symbols and error rate were analyzed.

The Rapid Information Processing Task (RIPT) is a widely used measure of sustained attention and working memory. Participants were presented with a series of single digits on a computer screen at a rate of 100 milliseconds for 10 minutes. They were instructed to press the space bar when presented with a target. The target sequences were defined as three consecutive odd digits or three consecutive even digits. Participants were presented with eight targets per minute, making a total of 80 targets in 10 minutes, with 5-30 digits between each target. The percentage of targets correctly detected (hit rate), and the mean reaction times on targets (in milliseconds) were analyzed.

The Smoking Stroop task assessed the attention-grabbing properties of cues (attentional bias). Participants were presented with words in different colors on a computer monitor. The participants were instructed to respond by pressing the color that corresponded with the word presented. They were instructed to respond as quickly as possible and to ignore the meaning of the words. Participants were presented with a block

of 33 neutral words (e.g., chair) and a block of 33 cigarette words (e.g., ashtray). The same task and scoring methods were used for this measure as those used by Waters et al. (2003).

Practice trials of the cognitive tasks and a baseline electroencephalogram occurred at the orientation session (except the Stroop task).

Data Analysis

To address specific aim 1 (between-race differences in withdrawal), an abstinence-induced change score (score when abstinent – score when non-abstinent) was calculated for each measure. This score captures the change in a measure as a result of abstinence, and is the primary outcome variable (Leventhal et al., 2007; Leventhal et al., 2010). This method is consistent with previous studies on tobacco withdrawal (Hughes, 2007b).

An independent samples *t*-test was computed for each difference score. Race was the independent variable and each abstinence-induced change score was the dependent measure. A significant *t*-value would indicate that Caucasians and African Americans differed in withdrawal. Consistent with Leventhal et al. (2007), independent sample *t*-tests were also conducted separately for each measure at each state (abstinent, non-abstinent). Again, race was the independent variable, and each cognitive, physiological, and self-report measure was the dependent variable. Cohen's *d* statistic (small $d = .20$, medium $d = .50$, large $d = .80$) was computed to interpret the magnitude of significant findings (Cohen, 1977). The same analytic procedures were used for specific aim 2 (effect of cigarette type on withdrawal).

For the abstinence-induced change scores, ANCOVAs were also conducted. For specific aim 1, race was the independent variable, and cigarettes per day and years of smoking were entered as covariates. Between-race differences in these covariates were observed and are reported in the results section.

Power analyses were conducted using G*Power 3.1 (Faul, Erdfelder, & Buchner, 2007). All power analyses used alpha = .05 and a two-tailed test. For specific aim 1, there was between 92% and 94% power to reject the null hypothesis if the true effect size in the population was a medium effect size (Cohen's d = 0.5). The variability was due to variation in sample size (n = 183 – 203) across the subjective, physiological, and cognitive variables (there were missing data on some measures). If the true effect size in the population was small (Cohen's d = 0.2), then there was much lower power to correctly reject the null hypothesis (between 27% and 29% power). For specific aim 2, for Caucasian smokers there was between 81% and 83% power to reject the null hypothesis (no effect of cigarette type) if the true effect size in the population was Cohen's $d = 0.6$.

CHAPTER 3: Results

Demographic and Smoking Variables

Consistent with the literature, African Americans smoked fewer cigarettes per day ($M = 20.8$, $SD = 6.7$) than Caucasians ($M = 23.7$, $SD = 6.2$), $t(199) = 2.07$, $p = .04$ (see Table 3). African Americans ($M = 38.8$, $SD = 9.6$) were significantly older than Caucasians ($M = 34.4$, $SD = 10.2$), $t(201) = -3.29$, $p = .001$. African Americans ($M = 21.2$, $SD = 10.3$) also reported that they had been smoking for more years than Caucasians ($M = 18.1$, $SD = 10.3$), $t(201) = -2.11$, $p = .02$ (Table 3). As expected, the two variables age and years of smoking were highly correlated ($r = .92$, $p < .001$). Consistent with the literature (Kabat, 1991; Giovino et al., 2004), African Americans were more likely to smoke menthol cigarettes, χ^2 (1, N=203) = 69.66, $p < .001$. In this sample approximately 92% of African Americans smoked menthol cigarettes compared to 42% of Caucasians.

Subjective Variables

Between-race differences on data from the abstinent condition, the non-abstinent condition, and the abstinence-induced change score (the primary outcome variable) are reported in Table 3. For all of these measures, African-Americans reported smaller abstinence induced increases in craving and withdrawal than Caucasians. A significant between-race difference in the abstinence-induced change score was observed for the following subjective variables (Table 4): MNWS craving, $t(200) = 2.09$, $p = .04$; WSWS total score, $t(201) = 3.41$, $p < .001$ (Figure 1); all WSWS subscale scores except Sadness (see Table 4); QSU total score, $t(200) = 2.50$, $p = .01$ (Figure 2); and QSU Factor 1, $t(200) = 2.54$, $p = .01$.

When controlling for cigarettes per day and years of smoking using ANCOVA, a significant *F* value for race was obtained for WSWS total score, WSWS Craving, WSWS Anger, QSU total score and QSU Factor 1 (Table 4). Again, for all of these measures, African Americans reported smaller abstinence-induced increases in craving and withdrawal than Caucasians.

The effect of race on the abstinent and non-abstinent conditions was also assessed. There were differences by race at the non-abstinent session on the WSWS Total score, the QSU Total score the WSWS Craving scale, WSWS Hunger scale, PANAS, and SBQ. African Americans reported higher ratings on the QSU Total Score t (200) = -2.43, p = .02; WSWS Total Score, t(201) = -2.49, p = .01; WSWS Craving, t(201) = -2.64, p = .008 PANAS, t(201) = -3.25, $p < .001$; and SBQ t(184) = -3.86, $p < .001$; and the WSWS Hunger scale, t(201) = -3.72 , $p < .001$ (there were no differences at the abstinent session on these measures).

In summary, African-Americans reported smaller abstinence induced increases in craving and withdrawal than Caucasians but higher withdrawal and craving during the non-abstinent session.

Physiological Variables

There were no significant between-race differences on the abstinence-induced change scores on the physiological measures (i.e., no Race X State interaction; Table 5). However, there were significant racial differences between the abstinent and non-abstinent conditions. Differences in systolic and diastolic blood pressure were observed, with African Americans reporting higher systolic and diastolic blood pressure than Caucasians during the non-abstinent condition, t(200) = -3.64, $p < .001$ and t(201) = -

4.06, $p < .001$, respectively. Similar differences were observed during the abstinent condition. African Americans reported higher systolic and diastolic blood pressure than Caucasians, $t(200) = -4.22$ $p < .001$ and $t(200) = -3.82$ $p < .001$ respectively. There were no consistent effects of race on EEG measures during the abstinent or non-abstinent condition.

Cognitive Variables

There were no significant between-race differences on the abstinence-induced change scores for the cognitive measures (Table 5). Between-race differences on the Rapid Information Processing Task were observed in both the abstinent and non-abstinent condition. African Americans had lower hit rates in the abstinence condition, $t(200) = 2.70$, $p = .007$, and in the non-abstinent condition, $t(199) = 3.57$, $p < .001$ compared to Caucasians.

Caucasian Menthol vs. Caucasian Non-Menthol Smokers

To examine the effect of cigarette type, Caucasian menthol and non-menthol smokers were compared. There were 42 menthol smokers and 57 non-menthol smokers. First, differences in the demographic and smoking variables were tested using independent sample t-tests. The demographic and smoking variables were the same as those variables included in the primary analysis (Table 2). Significant differences were observed for age and minutes to first cigarette. Caucasian menthol smokers were younger, $t(97) = 2.23$, $p = .03$ and smoked their first cigarette earlier in the day χ^2 (2, N = 99) = 11.58, $p = .003$. Given the small number of African American smokers who smoked non-menthol cigarettes (n = 4), differences between African American menthol and non-menthol could not be examined.

Next, the effect of cigarette type was examined for all study measures for Caucasians (Tables 6 and 7). Differences were observed on the PANAS positive scale. Caucasian menthol smokers reported a greater abstinence-induced change in positive affect, $t(97) = -2.34$, $p = .02$ compared to Caucasian non-menthol smokers. There were no other differences observed on abstinence-induced change scores.

CHAPTER 4: Discussion

The main finding of the study was that there was no evidence that African Americans experience greater nicotine withdrawal than Caucasians. In fact, contrary to hypothesis, African Americans reported smaller abstinence-induced changes in withdrawal on some self-report measures. There were no differences on cognitive and physiological measures. The finding that African Americans reported smaller abstinence-induced changes on subjective measures is consistent with a study of racial differences in withdrawal in adolescent smokers (Riedel, Robinson, Klesges, & McLain-Allen, 2003).

RACE DIFFERENCES IN WITHDRAWAL

Interestingly, the observed between-race differences in abstinence-induced changes in craving and withdrawal appear to be driven by African Americans reporting significantly greater craving and withdrawal at the non-abstinent session. The finding that African Americans reported higher craving on a number of measures, including the QSU total score, is consistent with findings from a study of racial differences in craving that used ecological momentary assessment (Carter et al., 2010). This finding is also noteworthy because craving plays an important role in the maintenance of nicotine dependence and is a predictor of relapse (Shiffman et al., 1997). Therefore, African Americans may benefit from treatment that emphasizes craving reduction such as nicotine replacement therapy (Shiffman, 2003). This is important because African Americans are less likely to utilize nicotine replacement therapy than Caucasians (Fu et al., 2005; Trinidad et al., 2011).

Prospective studies assessing the association between craving and cessation in African Americans are warranted.

Another possible explanation for the between-race difference in craving and withdrawal on abstinence-induced change scores is that responses on the abstinence condition could have been near or at ceiling, meaning that African Americans would have been constrained in their ability to report large increases in craving and withdrawal. However, the mean WSWS total score for African Americans at the abstinent session was 2.05 (on a 0 to 4 scale), meaning that their mean WSWS total score was only halfway along the range. The mean QSU total score for African Americans was 3.39 (on a 0 to 5 scale), meaning that there were 1.61 units between the mean score and the maximum score. These observations suggest it is unlikely that ceiling effects were responsible for the observed pattern of data.

Although there were significant effects of abstinence state on the objective measures that were used (Leventhal et al., 2010), there were no between-race differences in abstinence-induced change scores on objective measures. However, some significant effects of race were observed on the data from the non-abstinent and abstinent conditions. For example, African Americans exhibited higher blood pressure than Caucasians in both conditions. Although the effect of race on blood pressure was not germane to the research questions, this finding is consistent with the literature (Fiscella & Holt, 2008).

MENTHOL AND WITHDRAWAL

As noted in the introduction, there has been a growing interest in the effect of menthol on tobacco use, cessation, and illness, particularly in minorities and adolescents. In the current study, African Americans were much more likely to smoke menthol

cigarettes than were Caucasians. This finding is consistent with the literature. Given the small number of African American smokers in the sample who smoked non-menthol cigarettes, the analyses focused on the effect of cigarette type in Caucasian smokers. These analyses suggested that menthol had little effect on withdrawal in Caucasian smokers. There were no consistent differences between Caucasian menthol and Caucasian non-menthol smokers on abstinence-induced change scores.

Interestingly, menthol-related differences were observed for minutes to first cigarette. Menthol smokers smoked more quickly within waking when compared to non-menthol smokers. This finding is important because minutes to first cigarette, as assessed on the FTND, has been shown to predict smoking cessation outcomes (Baker et al., 2007). Future research should assess the implications of differences in time to first cigarette in menthol and non-menthol smokers.

LIMITATIONS

The study had a number of limitations. First, abstinence was limited to 12 hours because the parent study was not designed to examine between race differences in withdrawal. Different results might be obtained if participants were assessed during more protracted periods of abstinence. For example, given that African Americans eliminate nicotine more slowly than Caucasians, it is possible that they have higher levels of cotinine in their blood after 12-hr abstinence, and are more protected from the nicotine withdrawal syndrome during early abstinence (e.g., Keenan et al., 1994). However, given that there is conflicting evidence as to whether cotinine alleviates withdrawal (Hatsukami, Grillo, Pentel, Oncken, & Bliss, 1997), and given that any between-race differences in the half-life of nicotine are likely small (Perez-Stable et al., 1998), it seems

unlikely that the relatively modest between-race difference in nicotine clearance would have an impact on between-race differences on acute withdrawal symptoms.

Second, the study was not powered to detect small effect sizes (the parent study was not designed to assess between race differences or look at the effect of menthol on withdrawal). In addition, the study had very low power to detect an effect of menthol within African Americans because the sample only contained four African Americans who did not smoke menthol cigarettes. Therefore, these analyses were unable to be conducted.

Third, because this was an exploratory, hypothesis-generating study, there was no control for multiple tests, and therefore the family-wise error rate was elevated. An elevated family-wise error rate could potentially affect the observed between race differences in the non-abstinent condition. However, the consistency in the pattern of data on the total scores on the QSU and the WSWS bolsters confidence that African Americans truly experience greater craving and withdrawal when non-abstinent.

Fourth, at least for African Americans, the number of cigarettes per day in this sample was not representative of the general population. Studies indicate that 50% of African Americans are light smokers (smoking less than 10 cigarettes per day), compared to 20% of the general population (Okuyemi, Harris Scheibmeir, Choi, Powell, & Ahluwalia, 2002). The present analysis provided a withdrawal profile of heavy smokers. Future research should investigate nicotine withdrawal in light and moderate smokers.

Fifth, the sample was a non-treatment seeking sample. Therefore, our data may not generalize to the experience of smokers who are attempting cessation. Future studies should examine between-race differences in withdrawal for smokers wishing to quit.

Sixth, an additional concern is the stability of menthol preference among smokers. As noted by Giovino (2004), studies investigating menthol effects are limited by misclassification bias. The current study assessed menthol status by having participants identify their current cigarette brand and select if their brand was of the menthol variety. Although previous studies have suggested that menthol preference is stable (Murray, Connett, Skeans, & Tashkin, 2007), past history of menthol smoking was not directly assessed in this study. Future studies should assess current and past use of menthol products with greater precision.

Seventh, the analyses of the effects of race and menthol did not control for socioeconomic status (SES). A measure of SES was not collected in the parent study. SES is sometimes entered as a covariate in studies examining race and smoking because there is evidence that African Americans have higher rates of low-income households (Gilman, Abrams, & Buka, 2003) and because lower SES is associated with poorer cessation outcomes (Businelle et al., 2010). *A priori*, in the current study it might be expected that SES would be associated with worse outcomes: Individuals with lower SES would be expected to exhibit greater withdrawal. Yet, smaller abstinence-induced changes were found among African American smokers, who were potentially of lower SES. It is therefore unlikely that that the observed association between race and withdrawal was confounded by SES.

Last, the study was not well designed to examine the joint effects of race and cigarette type (i.e., compare African-American menthol vs. African-American non-menthol). As noted in the introduction, some authors have argued that the effect of cigarette type on smoking outcomes is moderated by race, such that there is an effect of

menthol for African American smokers but not for Caucasian smokers. Given the small number of African Americans who smoked non-menthol cigarettes, the study was not well designed to examine this hypothesis. Future studies could use much larger sample sizes to ensure that there are adequate numbers of participants in each cell (African American menthol smokers; African American non-menthol smokers; Caucasian menthol smokers; Caucasian non-menthol smokers). Alternatively, future researchers could recruit participants such that equal numbers were recruited in each of the fours cells. A potential disadvantage of the latter strategy is that the results may be less generalizable to the broader African American population.

STRENGTHS

The study also had strengths. First, to the author's knowledge, this is the first study to examine the effects of race and menthol on early abstinence in adult smokers. Second, the study included a battery of self-report, physiological, and cognitive measures. These measures These measures allowed for a comprehensive assessment of withdrawal. Third, the study measures have been shown to be sensitive to acute abstinence (Leventhal et al., 2010). In addition, robust gender differences in withdrawal have been reported in the same dataset (Leventhal et al., 2007), demonstrating that it is possible to detect associations between a dichotomous variable and abstinence-induced changes on the study measures.

SUMMARY

In sum, there was no evidence that African Americans experience greater acute tobacco withdrawal than Caucasians, or that Caucasian menthol smokers experience greater acute tobacco withdrawal than non-menthol smokers. Racial

differences in smoking cessation are unlikely to be explained by withdrawal. We also found that African Americans reported smaller abstinence-induced changes on subjective measures. Future research should further examine this finding.

Table 1. Review of Cessation Studies

Author	Population	Study Type	Analysis	Results	Notes
Trinidad et al., 2011	n = 141,603 C: 71.5% AA: 11.5% As/P.I : 4.5% H. :12.5%	**(S)** Tobacco Use Supplement to the Current Population Survey - Current Vs. Former Smoker	Logistic regression IV: Race DV: Cessation	Fewer AA reported being a former smoker 30% vs. 42 % ($p < .05$) **Odds of quitting for at least 6 mos. = .51*** for AA vs. C	
Rabius et al., 2011 (study 1)	n = 3,522 C: 85% AA: 15%	**(I)**RCT: Quit-line self-help materials vs. counseling	IV: Race DV: Cessation: at 7 month follow-up	**No difference in Cessation** AA: 17% C: 21% $p >. 05$	
Rabius et al., 2011 (study 2)	*Louisiana,* n=4954 C: 66%, AA: 34% *Texas,*n=5209 C: 76%, AA: 24% *District of Columbia* n=1648 C: 5%, AA: 95%	**(I)** ACS Quit-line	IV: Race DV: Cessation at 7 month follow-up	**No race difference in cessation rates** TX: 4% vs. 27%, LA: 29% vs. 27%, D.C. 23% vs. 23% $p > .05$	
Piper et al., 2010 (study 1)	n= 1,504 C: 83.9% AA: 13.6% O: 2.5%	**(I)** Conditions: Bupropion, nicotine lozenge; nicotine patch; nicotine patch + nicotine lozenge; bupro-pion + nicotine lozenge; placebo.	Logistic Regression IV: Race DV: initial cessation, 8 weeks, 6 mos. (calculated for each treatment group and combined)	**Lower cessation among AA** Initial OR = .34 $p < .05$ 8 weeks: .41, $p < .05$ 6 months = .59 $p < .05$	

Piper et al., 2010 (study 2)	n = 1,346 C: 87% AA: 9.5% O: 3.5%	**(I)** Conditions: Bupropion, nicotine lozenge; nicotine patch; nicotine patch + nicotine lozenge; bupropion SR + nicotine lozenge	Logistic Regression IV: Race DV: initial cessation, 8 weeks, 6 mos. (calculated for each treatment group and combined)	**No difference in cessation** *p* >.05	Combined sample (Study 1 and Study 2): **lower rates among AAs at 8** weeks w/patch + lozenge condition 28.8% vs. 52.4%; *p* < .001)
Covey et al., 2008	n=559 C: 82% AA: 5% H: 13%	**(I)** All : 8 weeks of treatment of Bupropion Nicotine Patch Counseling	IV: Race DV: Abstinence 4 weeks after treatment	**Rates of cessation, lower among AAs:** *OR* = .44 for AA, p < .05 *OR*= .46 for H, p < .05	
Fu et al., 2008a	n =1019 C: 33.2% AA: 29.8% Amer. In. 28.8% As. 8.5%	**(I)** Minnesota Health Care Programs database Use of NRT among low income smokers -7 day and 30 day abstinence	Logistic Regression IV: Race DV: Quit	**No significant race effect at 7 or 30 days.** at 7 days: C: 13.8%, AA: 13.6%, Amer. In.: 14.1, As. 20.1%, p > .05	All participants used NRT.
Fu et al., 2008b	n = 9,216 C: 86% AA: 10% H: 3% As.A: 1%	**(S)** Collaborative Study of the Genetics of Nicotine Dependence Current vs. Former Smoker	Logistic Regression IV: Race DV: Quit, NRT	*__Lower Rates among AA vs. C., OR = .66__ *p* < .05 *Not sig. for H or As. A	The sample consisted primarily of individuals with health insurance with lower than national average rates of lifetime and current smoking.
Trinidad et al., 2005	AA, H, C. n = 61,848 to 93,5554	**(S)** The California Tobacco Surveys Years: 1990, 1993 1996, 1999, 2002	Comparisons by Age, 18-29 , 30 - 45, 45+ (for each year Quit Ratios compared for all groups	**Successful cessation (+5 yrs) was lower among AA in all age groups** *p* < .05	*sample size varies by year *Greatest differences among 30-45 45+

King et al., 2004	n = 240, 488 C: 209,828 AA: 30,660	**(S)** Cross-sectional: National Health Interview Survey (1990 – 2000)	Logistic Regression IV: Race DV: Quit Proportion of Quitters	AA: 14.6 vs. W: 25.8 **Lower rates of former smokers among AAs** $p < .05$	*After adjusting for covariates disparity reduced

Note. C = Caucasian, AA = African American, H = Hispanic, Amer. In. = American Indian, As. A = Asian American, O = Other, S = Survey Study, I = Intervention

Table 2. Procedure and Timeline for Experimental Sessions

Procedure	Assessments	Time (min)	Questionnaire Wording
Exhaled CO	CO	2	-
Heart Rate/Blood Pressure	HR, SBP/DBP	1	-
Questionnaires (1)	PANAS, HQ, MNWQ, WSWS, SBQ	10	"so far today"
	QSU	4	"right now"
Cognitive Performance Tasks	ST, MT, DSST, RIPT	16	-
Questionnaires (2)	N/A	6	-
Attentional Bias Tasks	Smoking Stroop Task[1]	6	-
	Visual Probe Task	10	-
EEG	Electrode Placement	10	
	Eyes Closed	1	-
	Eyes Open	1	-

Note. Assessments are listed in the order they were completed. CO = carbon monoxide; HR = Heart Rate; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; PANAS = Positive and Negative Affect Scale; HQ = Hunger Questionnaire; MNWQ = Minnesota Nicotine Withdrawal Questionnaire; WSWS = Wisconsin Smoking Withdrawal Scale; SBQ = Subjective Bias Questionnaire; QSU = Brief Questionnaire of Smoking Urges ; ST = Two-Letter Search Task; MT = Serial Math Test; DSST = Digit Symbol Substitution Task; RIPT = Rapid Information Processing Task; EEG = Electroencephalogram. See text for further details. [1]Order of completion of Stroop and Picture Probe tasks was counterbalanced across subjects. There were two versions of the visual probe task, and participants were randomly assigned to task type. Data from the visual probe task are not reported here. N/A = Data from questionnaire administered at time 2 are not reported in the current study

Table 3. Baseline Sample Characteristics

	Caucasians (n = 99)	African Americans (n = 104)	All (N = 203)	t/χ^2
Age	34.4 (10.2)	38.8 (9.6)	36.7 (10.1)	-3.29*
Gender (%)				ns
Male	52.5	47.1	49.8	
Female	47.5	52.9	50.2	
SCL-90	47.8 (11.8)	48.8 (10.9)	48.2 (11.3)	ns
Cig/day	23.7 (6.2)	20.7 (6.7)	22.2 (6.6)	2.97*
FTND	6.6 (1.8)	6.4 (1.6)	6.5 (1.7)	ns
Years Smoking	18.1 (10.3)	21.2 (10.3)	19.5 (10.3)	-2.11*
Min until first cig (%)				ns
0-5	58.6	55.8	57.1	
6-30	39.4	41.4	40.4	
31+	2.0	2.9	2.5	
Cigarette Type (%)				69.77*
Menthol	42.4	96.1	69.9	
Non-menthol	57.6	3.9	30.0	

Note. Data are Mean (*SD)* unless otherwise noted; SCL-90 = Symptom Check List-90-Revised global severity index; FTND = Fagerström Test of Nicotine Dependence; *$p < .05$

Table 4. Subjective Measures by Race

	Non-Abstinent					Abstinent					Abstinence-induced Change[b]						
	C	AA	t	df	d	C	AA	t	df	d	C	AA	t	df	d	F	F cov.
MNWS (0-5)																	
Total	0.69	0.77	ns	201	-	1.87	1.83	ns	200	-	1.18	1.05	ns	200	-	1.05	0.27
Craving	2.09	2.42	ns	200	-	4.11	4.09	ns	200	-	2.02	1.58	2.09*	200	.30	4.36*	1.78
Irritable/angry	0.51	0.55	ns	201	-	2.37	2.29	ns	200	-	1.86	1.72	ns	200	-	0.30	0.02
Anxious/tense	0.76	0.77	ns	201	-	2.49	2.34	ns	197	-	1.74	1.56	ns	197	-	0.57	0.02
Concentration	0.59	0.60	ns	201	-	1.77	1.66	ns	200	-	1.18	1.06	ns	200	-	0.29	0.01
Restlessness	0.71	0.75	ns	201	-	2.05	1.82	ns	200	-	1.23	1.07	ns	200	-	1.17	1.02
Impatient	0.73	0.85	ns	199	-	2.35	2.33	ns	199	-	1.66	1.44	ns	197	-	0.75	0.41
Hunger	0.72	1.09	-2.02[a]*	201	.28	1.96	2.19	ns	200	-	1.23	1.08	ns	200	-	0.33	0.00
Autonomic	0.11	0.15	ns	201	-	0.26	0.87	ns	200	-	0.23	0.32	ns	200	-	0.38	0.64
Eating	0.27	0.87	ns	200	-	1.49	1.93	ns	200	-	1.22	1.06	ns	200	-	0.52	0.00
Drowsiness	0.50	0.41	ns	201	-	0.65	0.78	ns	197	-	0.25	0.36	ns	199	-	1.19	0.42
Headaches	0.19	0.18	ns	201	-	0.61	0.46	ns	200	-	0.41	0.27	ns	200	-	0.95	1.13
WSWS (0-4)																	
Total	1.16	1.37	-2.49*	201	.35	2.17	2.05	ns	201	-	1.02	0.67	3.41*	201	.48	11.63	6.63*
Anger	0.76	1.01	ns	200	-	2.08	1.72	ns	201	-	1.26	0.71	3.20*	201	.45	10.25	5.45*
Anxiety	1.17	1.21	ns	201	-	2.19	1.95	ns	201	-	1.02	0.74	2.02*	201	.28	4.08*	2.40
Concentration	0.89	1.01	ns	201	-	1.85	1.61	ns	201	-	0.95	0.59	2.37*	201	.33	5.60*	2.17
Craving	1.52	1.87	-2.64*	201	.37	3.20	3.11	ns	201	-	1.68	1.25	2.88*	201	.40	8.35*	6.04*
Hunger	1.30	1.74	-3.72*	201	.52	2.06	2.18	ns	201	-	0.76	0.44	2.14*	201	.30	6.50*	2.47
Sadness	1.08	1.11	ns	201	-	1.59	1.48	ns	201	-	0.50	0.36	ns	201	-	1.60	0.23
QSU (0-5)																	
Total	1.40	1.80	-2.43[a]*	200	.34	3.40	3.39	ns	201	-	2.00	1.59	2.50*	200	.35	6.27*	5.00*
Factor 1	2.06	2.38	ns	200	-	4.43	4.25	ns	201	-	2.37	1.87	2.54*	200	.36	6.45*	5.81*
Factor 2	0.75	1.22	-3.27*	200	.46	2.38	2.53	ns	201	-	1.62	1.31	ns	200	-	3.36	2.15
PANAS (1-5)																	
PA	2.91	3.29	-3.25*	201	.45	2.67	3.09	-3.39*	201	.48	-0.24	-0.20	ns	201	-	0.13	0.03
NA	1.24	1.23	ns	201	-	1.80	1.70	ns	201	-	0.57	0.47	ns	201	-	1.76	0.57
HQ (1-10)	3.49	4.39	ns	201	-	4.81	5.20	ns	201	-	1.32	0.81	ns	201	-	3.24	1.70
SBQ (0-4)	1.09	1.50	-3.86*	184	.56	2.44	2.61	ns	185	-	1.35	1.12	ns	184	-	2.41	0.80

Note. Data in Abstinent, Abstinent, and Abstinence-Induced Change columns are means. *$p < .05$ (ds, ts for non-significant effects not shown). Due to missing data, sample sizes vary across analyses (Ns = 186 - 203). [a]Satterthwaite test was used due to unequal variances. [b]Abstinence-Induced Change = Abstinent - Non-Abstinent. C = Caucasian; AA = African-American; MNWS = Minnesota Nicotine Withdrawal Questionnaire (scale: 0-5); WSWS = Wisconsin Smoking Withdrawal Scale (scale: 0-4); QSU = Brief Questionnaire of Smoking Urges (scale: 0-5); SBQ = Subjective Bias Questionnaire (scale: 0-4); PANAS = Positive and Negative Affect Scale (scale: 1-5); HQ = Hunger Questionnaire (1-10). F value = ANOVA analysis on abstinence-induced change scores with no covariates (equivalent to t value); F Cov. = ANCOVA analysis on abstinence-induced change scores with years smoking and cigarettes per day included as covariates.

Table 5. Objective measures by Race

	Non-Abstinent					Abstinent					Abstinence-induced Change[b]						
	C	AA	t	df	d	C	AA	t	df	d	C	AA	t	df	d	F	F Cov.
HR (bpm)	79.77	80.29	ns	200	-	69.34	71.34	ns	200	-	-10.43	-8.86	ns	201	-	1.06	1.09
SBP (mmHg)	120.30	126.95	-3.64*	200	.51	119.26	127.34	-4.22*	200	.60	-1.04	0.37	ns	199	-	0.70	0.87
DBP (mmHg)	72.33	77.66	-4.08[a]*	201	.57	71.20	76.32	-3.82*	200	.54	-1.13	-1.44	ns	200	-	0.06	0.00
EEG eyes closed																	
Δ power	104.74	94.07	ns	185	-	127.47	133.70	ns	183	-	29.86	23.17	ns	191	-	0.01	0.25
θ power	73.53	62.50	ns	185	-	79.65	66.94	ns	181	-	16.76	17.65	ns	191	-	0.00	0.01
α power	188.52	157.53	ns	186	-	183.10	156.67	ns	184	-	-9.02	-4.29	ns	191	-	0.25	0.01
β1 power	45.44	38.38	ns	184	-	49.95	42.42	ns	180	-	4.68	6.07	ns	190	-	0.12	0.15
β2 power	8.01	6.91	ns	187	-	8.03	7.80	ns	181	-	0.70	1.05	ns	191	-	0.49	0.28
Δ frequency	2.68	2.70	ns	198	-	2.68	2.69	ns	193	-	0.01	0.00	ns	192		0.01	0.06
θ frequency	6.99	6.93	ns	198	-	7.00	6.95	ns	193	-	0.01	0.02	ns	192	-	0.07	0.32
α frequency	10.53	10.77	-2.79*	193	.40	10.47	10.65	ns	198	-	-0.06	-0.12	ns	192	-	1.42	1.14
β1 frequency	19.67	19.96	ns	198	-	19.92	19.97	-2.27*	193	.33	-0.21	-0.05	ns	192	-	3.04	2.18
β2 frequency	29.09	29.19	ns	193	-	29.14	29.30	ns	198	-	0.05	0.12	ns	192	-	1.31	0.31
EEG eyes open																	
Δ power	148.91	124.32	ns	183	-	150.75	151.54	ns	188		1.95	25.19	ns	198	-	1.31	2.40
θ power	60.80	51.03	ns	185	-	67.57	52.90	2.32*	184	.34	10.01	6.56	ns	197	-	0.65	0.69
α power	79.25	65.24	ns	186	-	85.00	69.68	ns	189	-	7.59	4.78	ns	198	-	0.10	0.55
β1 power	23.48	16.83	ns	186	-	38.03	34.37	ns	184	-	4.00	5.00	ns	197	-	0.07	0.01
β2 power	8.60	8.24	ns	185	-	8.12	9.18	ns	187	-	-0.29	1.34	ns	198	-	1.36	1.03
Δ frequency	2.66	2.63	ns	198	-	2.72	2.64	3.02*	199	.43	0.06	0.01	ns	198	-	2.47	1.51
θ frequency	6.79	6.81	ns	198	-	6.78	6.79	ns	199	-	0.02	0.02	ns	198	-	0.01	0.01
α frequency	10.97	11.17	-2.73*	199	.39	10.89	11.01	ns	199	-	0.39	0.41	ns	198	-	1.60	1.74
β1 frequency	20.24	20.21	ns	198	-	19.98	20.10	ns	198	-	-0.26	-0.12	ns	198	-	2.35	2.10
β2 frequency	29.22	29.31	ns	198	-	29.28	29.43	-2.32*	199	.35	0.05	0.11	ns	198	-	0.87	0.81
RIPT																	
Hit (%)	0.54	0.48	2.70*	200	.38	0.53	0.45	3.57*	199	.51	-0.02	-0.03	ns	199		0.42	0.32
RT (ms)	524.50	551.31	ns	200	-	540.97	583.57	-2.73*	199	.39	15.97	32.25	ns	199	-	1.48	1.09
ST															-		
RT (s)	5.22	5.11	ns	199	-	5.61	5.71	ns	200	-	0.41	0.59	ns	198	-	1.27	0.32

Errors (%)	6.38	6.60	ns	199	-	6.19	4.55	ns	200	-	-0.71	-2.11	ns	198	-	1.30	0.40
MT																	
RT (s)	1.85	2.02	ns	201	-	1.95	2.14	ns	200	-	0.09	0.12	ns	200	-	0.09	0.01
Errors (%)	15.76	25.30	-4.39*	201	.62	17.82	25.71	-3.50*	200	.49	2.15	0.41	ns	200	-	1.67	1.00
DSST																	
No. Correct	26.62	20.54	3.99*	199	.57	25.90	19.27	4.38*	198	.62	-1.28	-0.93	ns	198	-	0.08	0.12
Errors (%)	14.41	16.54	ns	199	-	16.27	19.97	ns	198	-	3.43	2.05	ns	198	-	0.13	0.01
Stroop																	
St. (ms)	31.94	53.98	ns	197	-	39.40	65.18	ns	197	-	4.60	9.96	ns	192	-	0.06	0.02
Acute (ms)	51.58	78.87	ns	198	-	80.20	117.2	ns	199	-	22.70	36.19	ns	193	-	0.20	0.05

Note. Data in Non-Abstinent, Abstinent, and Abstinence-Induced Change columns are means. [a]Satterthwaite test was used because of unequal variances. [b]Abstinence-Induced Change = Abstinent - Non-Abstinent. C = Caucasian; AA = African-American; HR = Heart Rate; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; EEG = Electroencephalogram; RIPT = Rapid Information Processing Task; ST = Two-Letter Search Task; MT = Serial Math Task; DSST = Digit Symbol Substitution Task; RT = Reaction Time; Stroop = Smoking Stroop task; st. = standard smoking Stroop effect (see Waters et al., 2003). EEG measured in microvolts. F value = ANOVA analysis on abstinence-induced change scores with no covariates (equivalent to t value); F Cov. = ANCOVA analysis on abstinence-induced change scores with years smoking and cigarettes per day included as covariates.

Table 6. Subjective Measures by Menthol

	Non-Abstinent					Abstinent					Abstinence-induced Change[b]						
	N-M	M	t	df	d	N-M	M	t	df	d	N-M	M	t	df	d	F	F Cov.
MNWS (0-5)																	
Total	0.66	0.72	ns	97	-	1.81	1.96	ns	97	-	1.15	1.24	ns	97	-	0.25	0.03
Craving	1.98	2.24	ns	97	-	4.16	4.05	ns	97	-	2.18	1.81	ns	97	-	1.60	2.63
Irritable/angry	0.46	0.60	ns	97	-	2.10	2.73	ns	97	-	1.65	2.14	ns	97	-	2.34	1.37
Anxious/tense	0.84	0.64	ns	97	-	2.41	2.59	ns	96	-	1.59	1.95	ns	96	-	1.39	0.77
Concentration	0.70	0.43	ns	97	-	1.72	1.83	ns	97	-	1.02	1.40	ns	97	-	1.36	0.82
Restlessness	0.68	0.74	ns	97	-	1.72	1.65	ns	97	-	1.39	1.29	ns	97	-	0.09	0.12
Impatient	0.67	0.81	ns	97	-	2.46	2.21	ns	96	-	1.80	1.49	ns	96	-	0.83	0.84
Hunger	0.74	0.71	ns	97	-	1.84	2.12	ns	97	-	1.11	1.40	ns	97	-	0.76	0.00
Autonomic	0.09	0.14	ns	97	-	0.35	0.33	ns	97	-	0.26	0.19	ns	97	-	0.12	0.17
Eating	0.29	0.24	ns	97	-	1.37	1.64	ns	97	-	1.09	1.40	ns	96	-	0.94	0.07
Drowsiness	0.39	0.64	ns	97	-	0.52	0.81	ns	94	-	0.13	0.17	ns	94	-	0.02	0.29
Headaches	0.12	0.29	ns	97	-	0.42	1.34	ns	97	-	0.30	0.57	ns	97	-	1.23	1.94
WSWS (0-4)					-												
Total	1.16	1.15	ns	97	-	2.17	2.18	ns	97	-	1.01	1.02	ns	97	-	0.00	0.41
Anger	0.73	0.81	ns	97		1.94	1.34	ns	97	-	1.21	1.45	ns	97	-	0.68	0.05
Anxiety	1.20	1.31	ns	97	-	2.32	2.01	ns	97	-	1.11	0.88	ns	97	-	1.02	2.43
Concentration	0.98	0.79	ns	97	-	1.85	1.83	ns	97	-	0.87	1.05	ns	98	-	0.64	0.24
Craving	1.46	1.60	ns	97	-	3.22	3.18	ns	97	-	1.76	1.57	ns	97	-	0.75	1.33
Hunger	1.29	1.30	ns	97	-	2.02	2.10	ns	97	-	0.73	0.80	ns	97	-	0.09	0.17
Sadness	1.07	1.10	ns	97	-	1.55	1.64	ns	97	-	0.48	0.54	ns	97	-	0.00	0.00
QSU (0-5)																	
Total	1.37	1.44	ns	97	-	3.41	3.39	ns	97	-	2.04	1.95	ns	97	-	0.15	0.52
Factor 1	1.99	2.16	ns	97	-	2.42	2.30	ns	97	-	2.41	2.33	ns	97	-	0.08	0.27
Factor 2	0.76	0.73	ns	97	-	4.40	4.48	ns	97	-	1.66	1.58	ns	97	-	0.15	0.54
PANAS (1-5)					-												
PA	2.91	2.91	ns	97	-	2.47	2.82	ns	97	-	-0.09	-0.44	-2.34*	97	.48	5.49*	4.90*
NA	1.23	1.24	ns	97	-	1.82	1.79	ns	97	-	0.59	0.55	ns	97	-	0.19	0.14
HQ (1-10)	3.45	3.53	ns	97	-	4.55	5.16	ns	97	-	1.62	1.10	ns	97	-	1.79	0.20
SBQ (0-4)	1.17	1.00	ns	94	-	2.33	2.57	ns	95	-	1.57	1.18	ns	97	-	4.52*	2.05

Note: Data in Abstinent, Abstinent, and Abstinence-Induced Change columns are means for Caucasians only. *$p < .05$ (ds, ts for non-significant effects not shown). Due to missing data, sample sizes vary across analyses (Ns = 186 - 203). [a]Satterthwaite test was used due to unequal variances. [b]Abstinence-Induced Change = Abstinent - Non-Abstinent. N-M = Non-menthol; M = Menthol; MNWS = Minnesota Nicotine Withdrawal Questionnaire (scale: 0-5); WSWS = Wisconsin Smoking Withdrawal Scale (scale: 0-4); QSU = Brief Questionnaire of Smoking Urges (scale: 0-5); SBQ = Subjective Bias Questionnaire (scale: 0-4); PANAS = Positive and Negative Affect Scale (scale: 1-5); HQ = Hunger Questionnaire (1-10). F value = ANOVA analysis on abstinence-induced change scores with no covariates (equivalent to t value); F Cov. = ANCOVA analysis on abstinence-induced change scores with minutes to first cigarette and age as covariates.

Table 7. Objective Measures by Menthol

	Non-Abstinent					Abstinent					Abstinence-induced Change[b]						
	N-M	M	t	df	d	N-M	M	t	df	d	N-M	M	t	df	d	F	F Cov.
HR (bpm)	78.79	81.11	ns	97	-	68.74	70.16	ns	97	-	-10.05	-10.95	ns	97	-	1.01	0.00
SBP (mmHg)	121.05	119.28	ns	97	-	119.26	119.26	ns	97	-	-1.79	-0.03	ns	97	-	0.69	1.39
DBP (mmHg)	73.00	71.54	ns	97	-	71.40	70.93	ns	97	-	-1.51	-0.62	ns	98	-	0.43	0.17
EEG eyes closed																	
Δ power	96.28	116.98	ns	94	-	131.63	136.20	ns	92	-	37.13	20.34	ns	95	-	1.43	2.05
θ power	65.97	86.20	ns	92	-	101.06	80.38	ns	91	-	15.25	18.74	ns	95	-	0.12	0.31
α power	163.50	222.81	ns	93	-	161.73	209.77	ns	92	-	-7.23	-2.76	ns	95	-	0.74	0.39
β_1 power	40.37	52.14	ns	93	-	43.90	57.29	ns	91	-	4.21	5.29	ns	95		0.24	0.18
β_2 power	7.80	8.29	ns	94	-	7.86	8.26	ns	91	-	0.40	1.08	ns	95	-	0.00	0.02
Δ frequency	2.69	2.67	ns	97	-	2.65	2.72	ns	95	-	-0.02	0.05	ns	95	-	2.05	2.86
θ frequency	6.99	7.01	ns	97	-	7.04	6.99	ns	95	-	-0.00	0.02	ns	95	-	0.25	0.34
α frequency	7.00	7.03	ns	95	-	10.51	10.42	ns	95	-	-0.09	-0.03	ns	95	-	0.89	0.90
β_1 frequency	20.06	19.72	-2.08*	97	0.42	19.81	19.53	ns	95	-	-0.23	-0.19	ns	95	-	0.08	0.00
β_2 frequency	29.07	29.12	ns	97	-	29.16	29.13	ns	95	-	0.08	0.00	ns	95	-	0.54	0.67
EEG eyes open																	
Δ power	136.90	165.85	ns	92	-	147.63	154.60	ns	93	-	13.27	-3.40	ns	97	-	1.47	2.19
θ power	50.47	75.00	3.11*	93	0.64	78.08	59.44	2.16	92	0.45	9.38	12.04	ns	97	-	0.03	0.00
α power	65.44	98.26	ns	93	-	71.75	101.80	ns	93	-	8.21	6.74	ns	97	-	0.02	0.82
β_1 power	31.87	39.47	ns	93	-	32.87	44.54	2.33*	93	0.48	2.35	6.21	ns	97	-	2.77	3.32
β_2 power	8.60	7.33	ns	93	-	7.43	9.00	ns	93	-	-0.98	0.63	ns	97	-	3.44	3.86
Δ frequency	2.66	2.66	ns	97	-	2.73	2.71	ns	97	-	0.06	0.07	ns	97		0.01	0.00
θ frequency	6.73	6.30	ns	97	-	6.77	6.83	ns	97	-	0.03	0.00	ns	97	-	0.88	0.19
α frequency	11.00	10.92	ns	97	-	10.90	10.86	ns	97	-	-0.10	-0.06	ns	97	-	0.57	0.13
β_1 frequency	20.41	20.02	-2.40*	97	0.49	20.14	19.77	-2.28*	97	0.46	-0.27	-0.25	ns	97	-	0.01	0.18
β_2 frequency	29.23	29.23	ns	97	-	29.30	29.26	ns	97	-	0.06	0.03	ns	97	-	0.11	0.02
RIPT																	
Hit (%)	0.57	0.52	ns	97	-	0.55	0.50	ns	96	-	-0.02	-0.02	ns	96	-	0.02	0.00
RT (ms)	519.55	532.37	ns	97	-	546.14	537.25	ns	96	-	17.70	13.58	ns	96	-	.01	0.05
ST																	
RT (s)	0.30	0.58	ns	95	-	5.64	5.60	ns	96	-	0.30	.05	ns	95	-	1.75	1.32

Errors (%)	-1.40	0.25	ns	95	-	6.30	6.14	ns	96	-	-1.39	0.25	ns	95	-	0.73	0.43
MT																	
RT (s)	1.86	1.84	ns	97	-	2.01	1.86	ns	96	-	0.15	0.02	ns	96	-	1.73	0.48
Errors (%)	16.59	14.61	ns	97	-	18.14	17.36	ns	96	-	1.55	3.00	ns	96	-	0.30	0.05
DSST																	
No. Correct	25.70	27.90	ns	96	-	25.82	26.02	ns	95	-	-0.23	-1.88	ns	95	-	0.66	0.80
Errors (%)	16.64	11.32	ns	96	-	17.67	14.36	ns	95	-	1.33	3.04	ns	95	-	0.11	0.05
Stroop																	
St. (ms)	18.89	49.35	ns	96	-	29.76	52.04	ns	95	-	6.10	2.68	ns	94	-	0.02	0.02
Acute (ms)	31.82	77.92	ns	96	-	58.22	108.9	ns	95	-	16.19	31.07	ns	94	-	0.14	0.06

Note. Data in Non-Abstinent, Abstinent, and Abstinence-Induced Change columns are means for Caucasians only. [a]Satterthwaite test was used because of unequal variances. [b]Abstinence-Induced Change = Abstinent - Non-Abstinent. N-M = Non-menthol; M = Menthol; HR = Heart Rate; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; EEG = Electroencephalogram; RIPT = Rapid Information Processing Task; ST = Two-Letter Search Task; MT = Serial Math Task; DSST = Digit Symbol Substitution Task; RT = Reaction Time; Stroop = Smoking Stroop task; st. = standard smoking Stroop effect (see Waters et al., 2003). EEG measured in microvolts. F value = ANOVA analysis on abstinence-induced change scores with no covariates (equivalent to t value); F Cov. = ANCOVA analysis on abstinence-induced change scores with minutes to first cigarette and age as covariates.

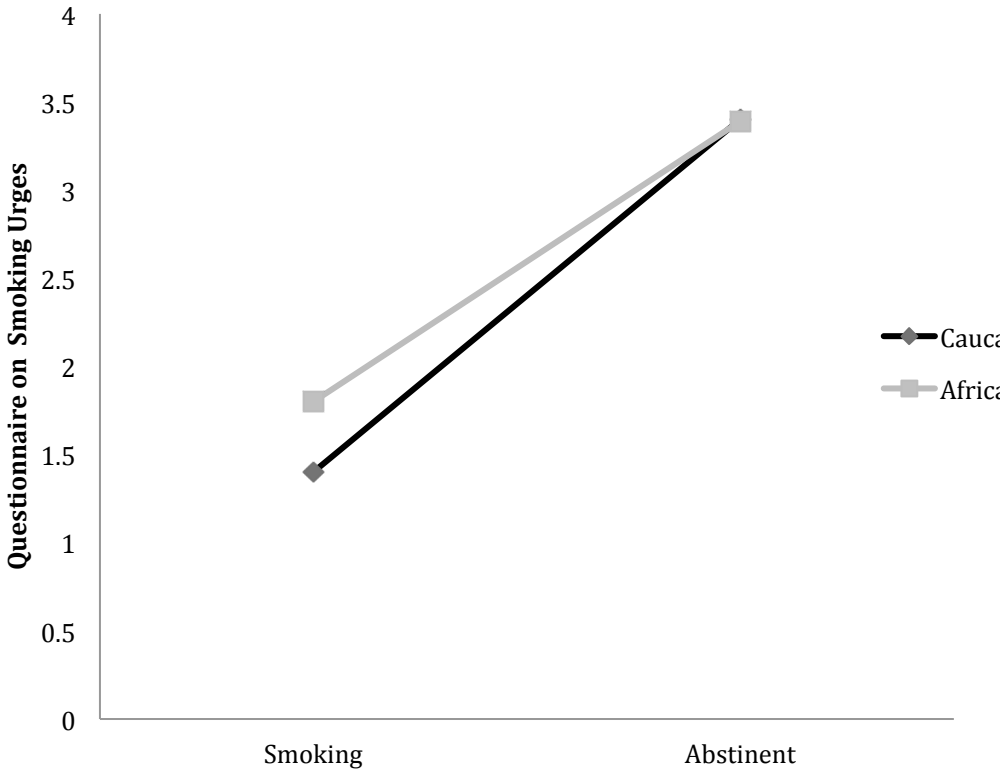

Figure 1: Questionnaire for Smoking Urges total score by race during the non-abstin
state and abstinent state

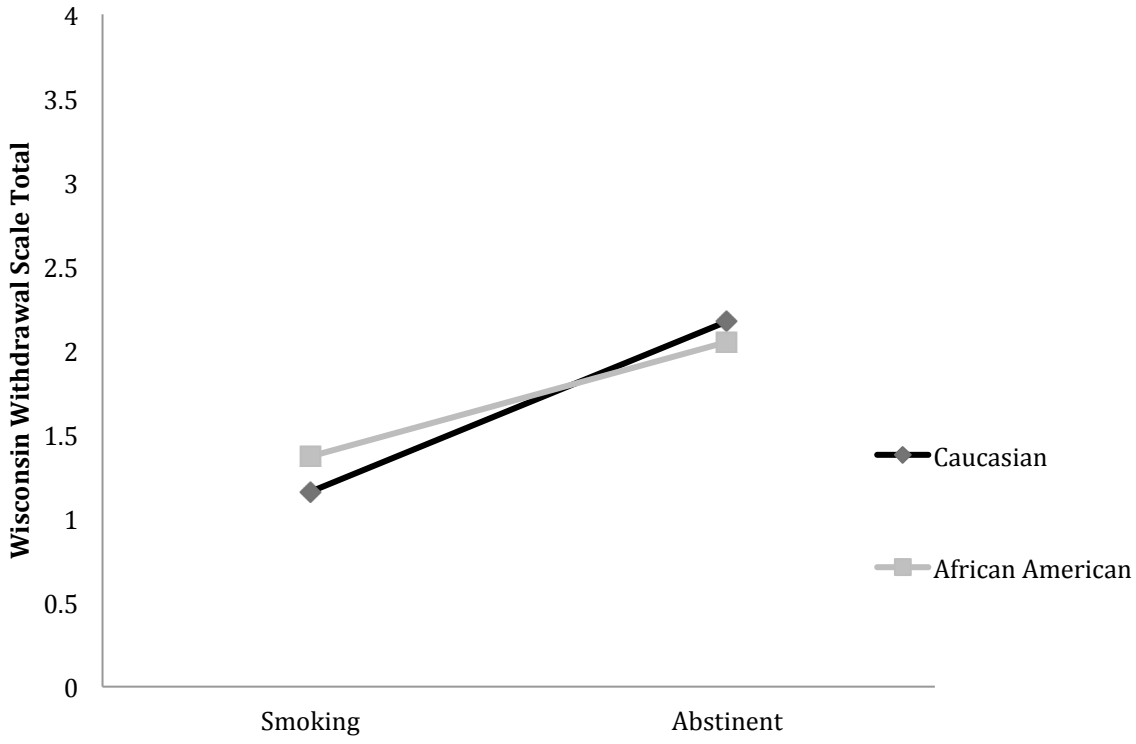

Figure 2: Wisconsin Smoking Withdrawal Scale total score by race during the non-abstinent state and abstinent state

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